

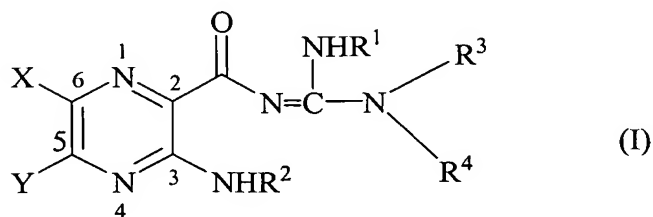
## IN THE CLAIMS

The status of each claim is listed below.

Claims 1-81: Canceled.

82. (Currently Amended) A method of effecting in a subject at least one member selected from the group consisting of promoting hydration of mucosal surfaces, promoting ocular hydration, promoting corneal hydration, promoting mucus clearance in mucosal surfaces, restoring mucosal defense, preventing ventilator-induced pneumonia, inducing sputum for diagnostic purposes, blocking sodium channels, treating chronic bronchitis, treating cystic fibrosis, treating sinusitis, treating vaginal dryness, treating dry eye, treating Sjogren's disease, treating distal intestinal obstruction syndrome, treating dry skin, treating esophagitis, treating dry mouth (xerostomia), treating nasal dehydration, treating chronic obstructive pulmonary disease, treating emphysema, treating pneumonia, treating constipation, treating chronic diverticulitis, treating rhinosinusitis, treating asthma, treating primary ciliary dyskinesia, and treating otitis media, comprising:

administering to the subject an effective amount of a compound represented by formula (I):



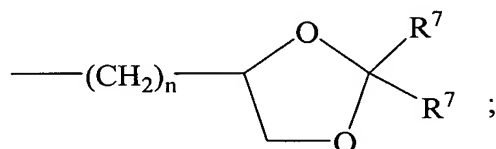
wherein

X is hydrogen, halogen, trifluoromethyl, lower alkyl, unsubstituted or substituted phenyl, lower alkyl-thio, phenyl-lower alkyl-thio, lower alkyl-sulfonyl, or phenyl-lower alkyl-sulfonyl;

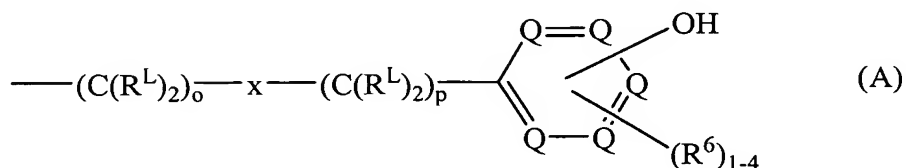
Y is hydrogen, hydroxyl, mercapto, lower alkoxy, lower alkyl-thio, halogen, lower alkyl, unsubstituted or substituted mononuclear aryl, or  $-N(R^2)_2$ ;

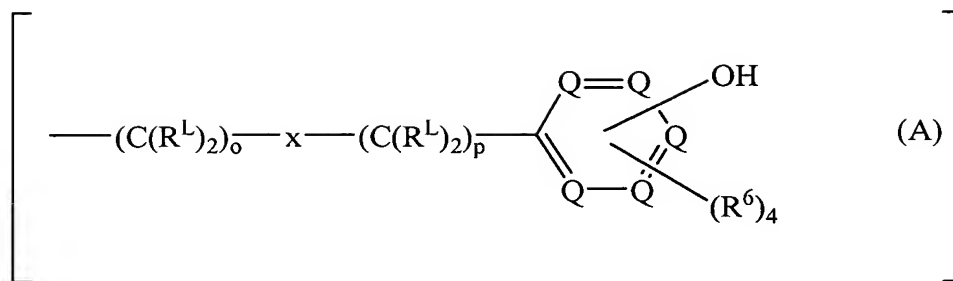
$R^1$  is hydrogen or lower alkyl;

each  $R^2$  is, independently,  $-R^7$ ,  $-(CH_2)_m-OR^8$ ,  $-(CH_2)_m-NR^7R^{10}$ ,  $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,  $-(CH_2CH_2O)_m-R^8$ ,  $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$ ,  $-(CH_2)_n-C(=O)NR^7R^{10}$ ,  $-(CH_2)_n-Z_g-R^7$ ,  $-(CH_2)_m-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,  $-(CH_2)_n-CO_2R^7$ , or



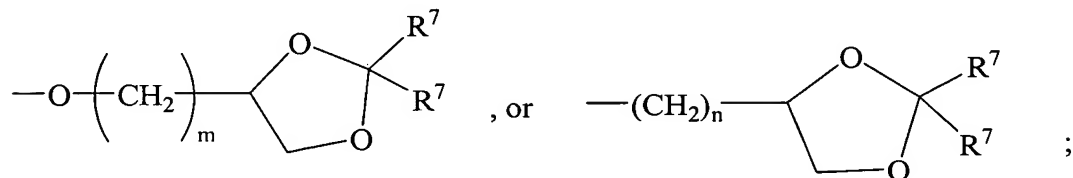
$R^3$  and  $R^4$  are each, independently, hydrogen, a group represented by formula (A), lower alkyl, hydroxy lower alkyl, phenyl, phenyl-lower alkyl, (halophenyl)-lower alkyl, lower-(alkylphenylalkyl), lower alkoxyphenyl)-lower alkyl, naphthyl-lower alkyl, or pyridyl-lower alkyl, with the proviso that at least one of  $R^3$  and  $R^4$  is a group represented by formula (A):





wherein

each  $\text{R}^{\text{L}}$  is, independently,  $-\text{R}^7$ ,  $-(\text{CH}_2)_n\text{OR}^8$ ,  $-\text{O}-(\text{CH}_2)_m\text{OR}^8$ ,  $-(\text{CH}_2)_n\text{NR}^7\text{R}^{10}$ ,  $-\text{O}-(\text{CH}_2)_m\text{NR}^7\text{R}^{10}$ ,  $-(\text{CH}_2)_n(\text{CHOR}^8)(\text{CHOR}^8)_n\text{CH}_2\text{OR}^8$ ,  $-\text{O}-(\text{CH}_2)_m(\text{CHOR}^8)(\text{CHOR}^8)_n\text{CH}_2\text{OR}^8$ ,  $-(\text{CH}_2\text{CH}_2\text{O})_m\text{R}^8$ ,  $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m\text{R}^8$ ,  $-(\text{CH}_2\text{CH}_2\text{O})_m\text{CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$ ,  $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m\text{CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$ ,  $-(\text{CH}_2)_n\text{C}(=\text{O})\text{NR}^7\text{R}^{10}$ ,  $-\text{O}-(\text{CH}_2)_m\text{C}(=\text{O})\text{NR}^7\text{R}^{10}$ ,  $-(\text{CH}_2)_n(\text{Z})_g\text{R}^7$ ,  $-\text{O}-(\text{CH}_2)_m(\text{Z})_g\text{R}^7$ ,  $-(\text{CH}_2)_n\text{NR}^{10}\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n\text{CH}_2\text{OR}^8$ ,  $-\text{O}-(\text{CH}_2)_m\text{NR}^{10}\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n\text{CH}_2\text{OR}^8$ ,  $-(\text{CH}_2)_n\text{CO}_2\text{R}^7$ ,  $-\text{O}-(\text{CH}_2)_m\text{CO}_2\text{R}^7$ ,  $-\text{OSO}_3\text{H}$ ,  $-\text{O-glucuronide}$ ,  $-\text{O-glucose}$ , or



each  $x$  is, independently,  $\text{O}$ ,  $\text{NR}^7$ ,  $\text{C}=\text{O}$ ,  $\text{CHOH}$ ,  $\text{C}=\text{N-R}^6$ , or represents a single bond;

each  $o$  is, independently, an integer from 0 to 10;

each  $p$  is, independently, an integer from 0 to 10;

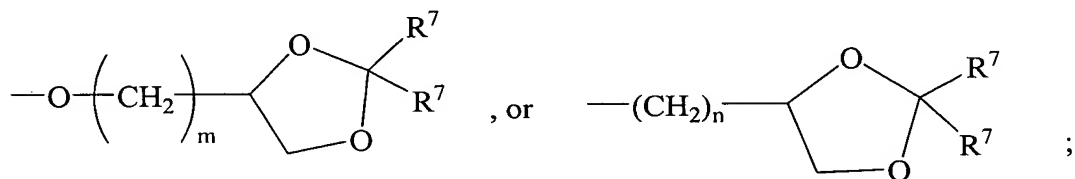
with the proviso that (a) the sum of  $o$  and  $p$  in each contiguous chain is

from 1 to 10 when  $x$  is  $\text{O}$ ,  $\text{NR}^7$ ,  $\text{C}=\text{O}$ , or  $\text{C}=\text{N-R}^6$  or (b) that the sum of  $o$  and  $p$

in each contiguous chain is from 4 to 10 when  $x$  represents a single bond;

each  $\text{R}^6$  is, independently,  $-\text{R}^7$ ,  $-\text{OH}$ ,  $-\text{OR}^{11}$ ,  $-\text{N}(\text{R}^7)_2$ ,  $-(\text{CH}_2)_m\text{OR}^8$ ,

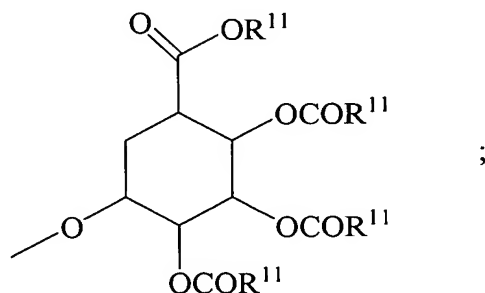
$-\text{O}-(\text{CH}_2)_m-\text{OR}^8$ ,  $-(\text{CH}_2)_n-\text{NR}^7\text{R}^{10}$ ,  $-\text{O}-(\text{CH}_2)_m-\text{NR}^7\text{R}^{10}$ ,  
 $-(\text{CH}_2)_n(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$ ,  $-\text{O}-(\text{CH}_2)_m(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$ ,  
 $-(\text{CH}_2\text{CH}_2\text{O})_m-\text{R}^8$ ,  $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m-\text{R}^8$ ,  $-(\text{CH}_2\text{CH}_2\text{O})_m-\text{CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$ ,  
 $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m-\text{CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$ ,  $-(\text{CH}_2)_n-\text{C}(=\text{O})\text{NR}^7\text{R}^{10}$ ,  
 $-\text{O}-(\text{CH}_2)_m-\text{C}(=\text{O})\text{NR}^7\text{R}^{10}$ ,  $-(\text{CH}_2)_n-(\text{Z})_g-\text{R}^7$ ,  $-\text{O}-(\text{CH}_2)_m-(\text{Z})_g-\text{R}^7$ ,  
 $-(\text{CH}_2)_n-\text{NR}^{10}-\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$ ,  
 $-\text{O}-(\text{CH}_2)_m-\text{NR}^{10}-\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$ ,  
 $-(\text{CH}_2)_n-\text{CO}_2\text{R}^7$ ,  $-\text{O}-(\text{CH}_2)_m-\text{CO}_2\text{R}^7$ ,  $-\text{OSO}_3\text{H}$ ,  $-\text{O-glucuronide}$ ,  $-\text{O-glucose}$ ,



wherein when two  $\text{R}^6$  are  $-\text{OR}^{11}$  and are located adjacent to each other on a phenyl ring, the alkyl moieties of the two  $\text{R}^6$  may be bonded together to form a methylenedioxy group;

each  $\text{R}^7$  is, independently, hydrogen or lower alkyl;

each  $\text{R}^8$  is, independently, hydrogen, lower alkyl,  $-\text{C}(=\text{O})-\text{R}^{11}$ , glucuronide, 2-tetrahydropyranyl, or



each  $\text{R}^9$  is, independently,  $-\text{CO}_2\text{R}^7$ ,  $-\text{CON}(\text{R}^7)_2$ ,  $-\text{SO}_2\text{CH}_3$ , or  $-\text{C}(=\text{O})\text{R}^7$ ;

each  $\text{R}^{10}$  is, independently,  $-\text{H}$ ,  $-\text{SO}_2\text{CH}_3$ ,  $-\text{CO}_2\text{R}^7$ ,  $-\text{C}(=\text{O})\text{NR}^7\text{R}^9$ ,

$-\text{C}(=\text{O})\text{R}^7$ , or  $-\text{CH}_2-(\text{CHOH})_n-\text{CH}_2\text{OH}$ ;

each  $\text{Z}$  is, independently,  $\text{CHOH}$ ,  $\text{C}(=\text{O})$ ,  $\text{CHNR}^7\text{R}^{10}$ ,  $\text{C}=\text{NR}^{10}$ , or  $\text{NR}^{10}$ ;

each  $R^{11}$  is, independently, lower alkyl;

each  $g$  is, independently, an integer from 1 to 6;

each  $m$  is, independently, an integer from 1 to 7;

each  $n$  is, independently, an integer from 0 to 7;

each  $Q$  is, independently,  $C-R^5$ ;  $C-R^6$ ; or a nitrogen atom, wherein at most three  $Q$  in a ring are nitrogen atoms;

or a pharmaceutically acceptable salt thereof, and

inclusive of all enantiomers, diastereomers, and racemic mixtures thereof.

83. (Previously Presented) The method of Claim 82, wherein promoting hydration of mucosal surfaces is effected.

84. (Previously Presented) The method of Claim 82, promoting ocular hydration is effected.

85. (Previously Presented) The method of Claim 82 promoting corneal hydration is effected.

86. (Previously Presented) The method of Claim 82, promoting mucus clearance in mucosal surfaces is effected.

87. (Previously Presented) The method of Claim 82, restoring mucosal defense is effected.

88. (Previously Presented) The method of Claim 82, preventing ventilator-induced pneumonia is effected.

89. (Previously Presented) The method of Claim 82, inducing sputum for diagnostic purposes is effected.

90. (Previously Presented) The method of Claim 82, blocking sodium channels is effected.

91. (Previously Presented) The method of Claim 82, treating chronic bronchitis is effected.

92. (Previously Presented) The method of Claim 82, treating cystic fibrosis is effected.

93. (Previously Presented) The method of Claim 82, treating sinusitis is effected.

94. (Previously Presented) The method of Claim 82, treating vaginal dryness is effected.

95. (Previously Presented) The method of Claim 82, treating dry eye is effected.

96. (Previously Presented) The method of Claim 82, treating Sjogren's disease is effected.

97. (Previously Presented) The method of Claim 82, treating distal intestinal obstruction syndrome is effected.
98. (Previously Presented) The method of Claim 82, treating dry skin, treating esophagitis is effected.
99. (Previously Presented) The method of Claim 82, treating dry mouth (xerostomia) is effected.
100. (Previously Presented) The method of Claim 82, treating nasal dehydration is effected.
101. (Previously Presented) The method of Claim 82, treating chronic obstructive pulmonary disease is effected.
102. (Previously Presented) The method of Claim 82, treating emphysema is effected.
103. (Previously Presented) The method of Claim 82, treating pneumonia is effected.
104. (Previously Presented) The method of Claim 82, treating constipation is effected.
105. (Previously Presented) The method of Claim 82, treating chronic diverticulitis is effected.

106. (Previously Presented) The method of Claim 82, treating rhinosinusitis is effected.

107. (Previously Presented) The method of Claim 82, treating asthma is effected.

108. (Previously Presented) The method of Claim 82, treating primary ciliary dyskinesia is effected.

109. (Previously Presented) The method of Claim 82, treating otitis media is effected.

110. (Previously Presented) The method of Claim 82, wherein the nasal dehydration is brought on by administering dry oxygen to the subject.

111. (Previously Presented) The method of Claim 82, wherein the compound is administered orally or via a suppository or enema.

112. (Previously Presented) The method of Claim 82, wherein Y is  $\text{-NH}_2$ .

113. (Previously Presented) The method of Claim 112, wherein  $\text{R}^2$  is hydrogen.

114. (Previously Presented) The method of Claim 113, wherein  $\text{R}^1$  is hydrogen.

115. (Previously Presented) The method of Claim 114, wherein X is chlorine.



116. (Previously Presented) The method of Claim 115, wherein  $R^3$  is hydrogen.
117. (Previously Presented) The method of Claim 116, wherein each  $R^L$  is hydrogen.
118. (Previously Presented) The method of Claim 117, wherein o is 4.
119. (Previously Presented) The method of Claim 118, wherein p is 0.
120. (Previously Presented) The method of Claim 119, wherein x represents a single bond.
121. (Previously Presented) The method of Claim 120, wherein each  $R^6$  is hydrogen.
122. (Previously Presented) The method of Claim 121, wherein at most one Q is a nitrogen atom.
123. (Previously Presented) The method of Claim 122, wherein no Q is a nitrogen atom.
- 124 (Previously Presented) The method of Claim 82, wherein
- X is halogen;
- Y is  $-N(R^7)_2$ ;
- $R^1$  is hydrogen or  $C_1$ - $C_3$  alkyl; and
- $R^2$  is  $-R^7$ ,  $-(CH_2)_m-OR^7$ , or  $-(CH_2)_n-CO_2R^7$ ;

$R^3$  is a group represented by formula (A); and

$R^4$  is hydrogen, a group represented by formula (A), or lower alkyl;

125. (Previously Presented) The method of Claim 124, wherein

X is chloro or bromo;

Y is  $-N(R^7)_2$ ;

$R^2$  is hydrogen or  $C_1$ - $C_3$  alkyl;

at most three  $R^6$  are other than hydrogen as defined above;

at most three  $R^L$  are other than hydrogen as defined above; and

at most 2 Q in a ring are nitrogen atoms.

126. (Previously Presented) The method of Claim 124, wherein Y is  $-NH_2$ .

127. (Previously Presented) The method of Claim 126, wherein

$R^4$  is hydrogen;

at most one  $R^L$  is other than hydrogen as defined above;

at most two  $R^6$  are other than hydrogen as defined above; and

at most 1 Q in a ring is a nitrogen atom.

128. (Previously Presented) The method of Claim 127, wherein no Q in a ring is a nitrogen atom.

129. (Previously Presented) The method of Claim 127, wherein x is O,  $NR^7$ ,  $C=O$ ,  $CHOH$ , or  $C=N-R^6$ .

130. (Previously Presented) The method of Claim 127, wherein x represents a single bond.

131. (Previously Presented) The method of Claim 82, wherein x is O,  $\text{NR}^7$ ,  $\text{C}=\text{O}$ ,  $\text{CHOH}$ , or  $\text{C}=\text{N}-\text{R}^6$ .

132. (Previously Presented) The compound of Claim 82, wherein x represents a single bond.

133. (Previously Presented) The compound of Claim 82, wherein each  $\text{R}^6$  is hydrogen.

134. (Previously Presented) The method of Claim 82, wherein at most two  $\text{R}^6$  are other than hydrogen as defined in Claim 82.

135. (Previously Presented) The method of Claim 82, wherein one  $\text{R}^6$  is other than hydrogen as defined in Claim 82.

136. (Previously Presented) The method of Claim 82, wherein one  $\text{R}^6$  is  $-\text{OH}$ .

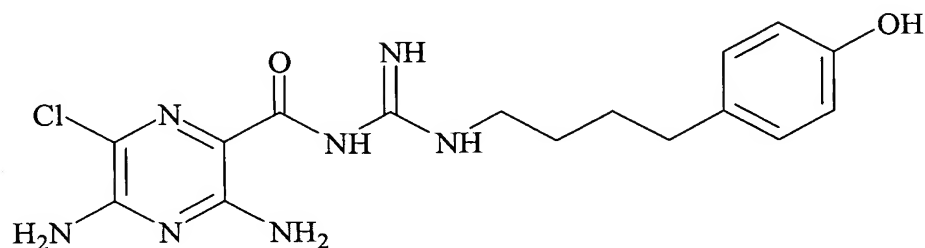
137. (Previously Presented) The method of Claim 82, wherein each  $\text{R}^L$  is hydrogen.

138. (Previously Presented) The method of Claim 82, wherein at most two  $\text{R}^L$  are other than hydrogen as defined in Claim 82.

139. (Previously Presented) The method of Claim 82, wherein one R<sup>L</sup> is other than hydrogen as defined in Claim 82.

140. (Previously Presented) The method of Claim 82, wherein x represents a single bond and the sum of o and p is 4 to 6.

141. (Previously Presented) The method of Claim 82, wherein the compound is represented by the formula

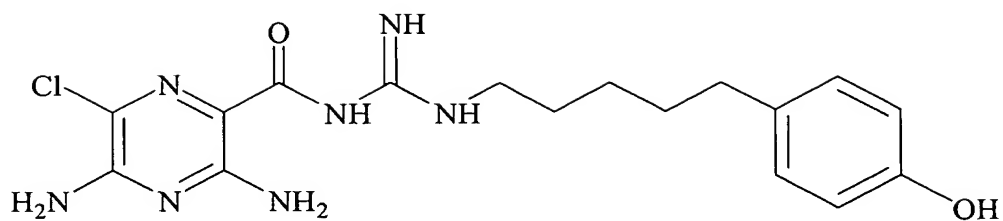


142. (Previously Presented) The method of Claim 141, wherein the compound is in the form of a pharmaceutically acceptable salt.

143. (Previously Presented) The method of Claim 142, wherein the compound is in the form of a hydrochloride salt.

144. (Previously Presented) The method of Claim 142, wherein the compound is in the form of a mesylate salt.

145. (Previously Presented) The method of Claim 82, wherein the compound is represented by the formula

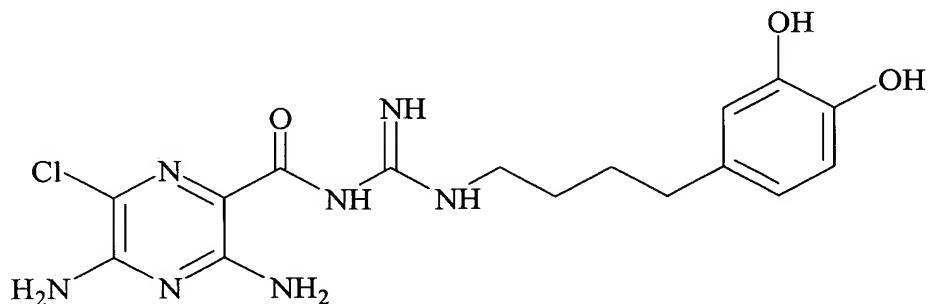


146. (Previously Presented) The method of Claim 145, wherein the compound is in the form of a pharmaceutically acceptable salt.

147. (Previously Presented) The method of Claim 146, wherein the compound is in the form of a hydrochloride salt.

148. (Previously Presented) The method of Claim 146, wherein the compound is in the form of a mesylate salt.

149. (Previously Presented) The method of Claim 82, wherein the compound is represented by the formula

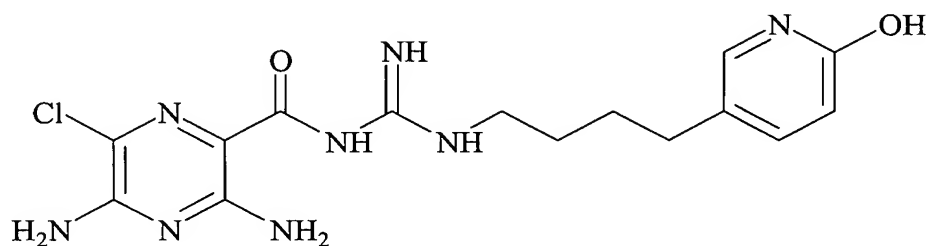


150. (Previously Presented) The method of Claim 149, wherein the compound is in the form of a pharmaceutically acceptable salt.

151. (Previously Presented) The method of Claim 150, wherein the compound is in the form of a hydrochloride salt.

152. (Previously Presented) The method of Claim 150, wherein the compound is in the form of a mesylate salt.

153. (Previously Presented) The method of Claim 82, wherein the compound is represented by the formula

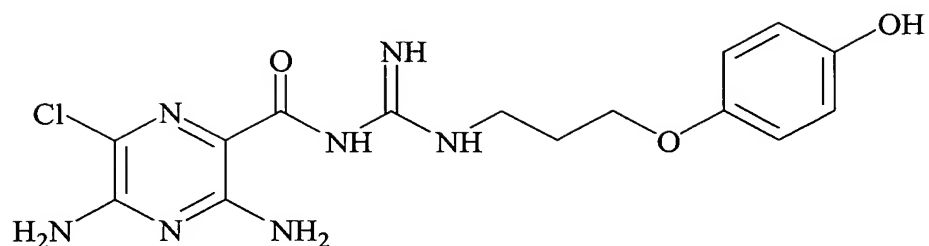


154. (Previously Presented) The method of Claim 153, wherein the compound is in the form of a pharmaceutically acceptable salt.

155. (Previously Presented) The method of Claim 154, wherein the compound is in the form of a hydrochloride salt.

156. (Previously Presented) The method of Claim 154, wherein the compound is in the form of a mesylate salt.

157. (Previously Presented) The method of Claim 82, wherein the compound is represented by the formula

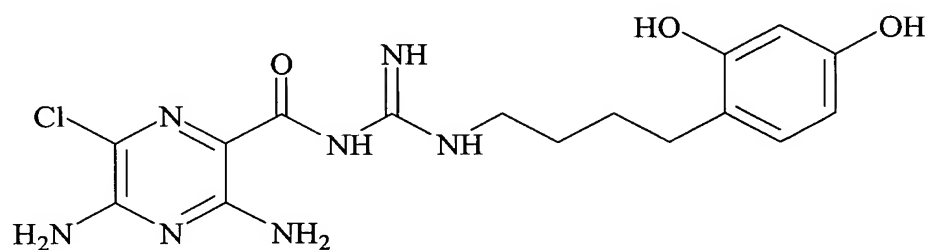


158. (Previously Presented) The method of Claim 157, wherein the compound is in the form of a pharmaceutically acceptable salt.

159. (Previously Presented) The method of Claim 158, wherein the compound is in the form of a hydrochloride salt.

160. (Previously Presented) The method of Claim 158, wherein the compound is in the form of a mesylate salt.

161. (Previously Presented) The method of Claim 82, wherein the compound is represented by the formula



162. (Previously Presented) The method of Claim 161, wherein the compound is in the form of a pharmaceutically acceptable salt.

163. (Previously Presented) The method of Claim 162, wherein the compound is in the form of a hydrochloride salt.

164. (Previously Presented) The method of Claim 162, wherein the compound is in the form of a mesylate salt.

165. (Previously Presented) The method of Claim 82, wherein the compound is in the form of a pharmaceutically acceptable salt.

166. (Previously Presented) The method of Claim 82, wherein the compound is in the form of a mesylate salt.

167. (Previously Presented) The method of Claim 82, wherein the compound is administered as a pharmaceutical composition which also comprises a pharmaceutically acceptable carrier.

168. (Currently Amended) The method of Claim 82, wherein the compound is administered as a composition which also comprises a P2Y2 receptor agonist inhibitor.

169. (Previously Presented) The method of Claim 82, wherein the compound is administered as a composition which also comprises a bronchodilator.